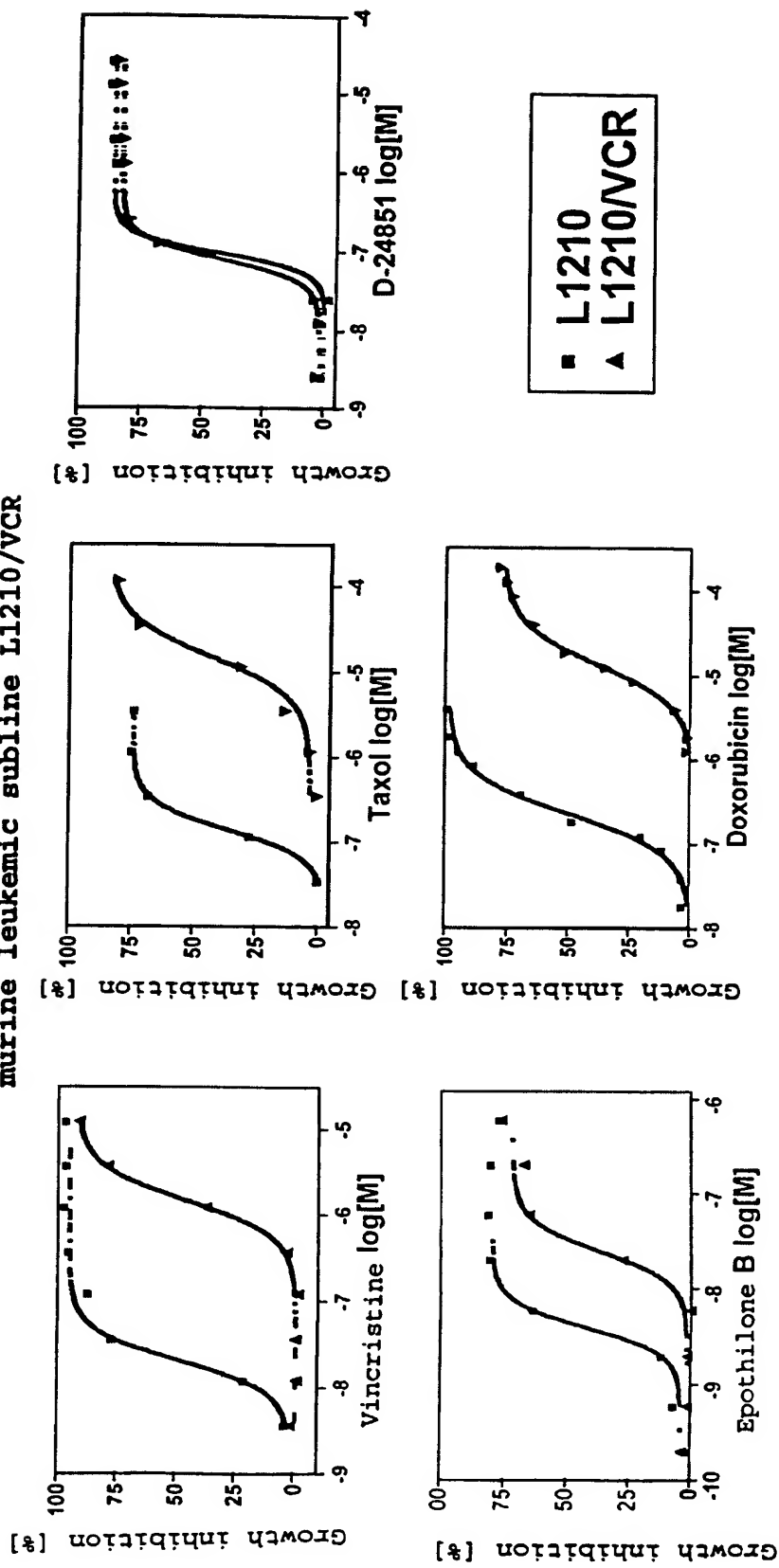


Cytotoxic action of D-24851 against MDR  
murine leukemic subline L1210/VCR

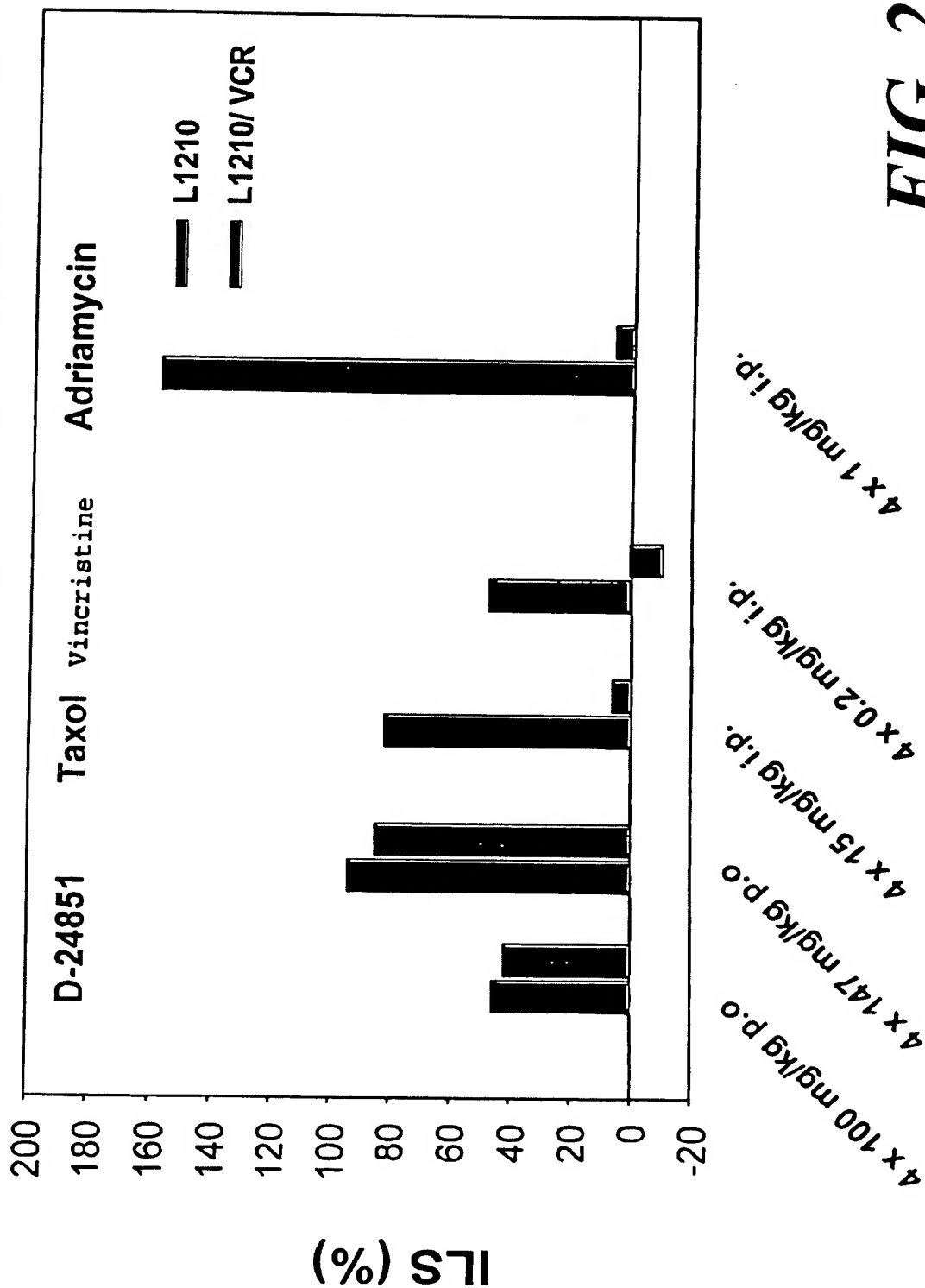


- In contrast to Taxol, doxorubicin, vincristine or epothilone B, D-24851 has the same cytotoxic activity against the MDR mouse leukemic subline L1210/VCR as against the normal

L1210

**FIG. 1**

# Action of D-24851 on a multidrug-resistant tumor



**FIG. 2**

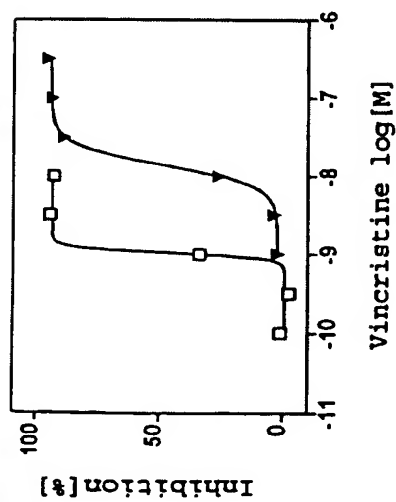
**Influence of D-24851 on the multidrug-resistant murine  
leukemia L1210 (dose 10% of the LD<sub>50</sub>)**

	<b>Dose (mg/kg)</b>	<b>L1210</b>	<b>L1210/VCR</b>
		<b>ILS %</b>	<b>ILS %</b>
<b>D-24851</b>	<b>4 x 100 p.o.</b>	<b>46</b>	<b>42</b>
	<b>4 x 147 p.o.</b>	<b>94</b>	<b>85</b>
<b>Adriamycin</b>	<b>4 x 1 i.p.</b>	<b>158</b>	<b>6</b>
<b>Taxol</b>	<b>4 x 15 i.p.</b>	<b>82</b>	<b>6</b>
<b>Vincristine</b>	<b>4 x 0.2 i.p.</b>	<b>47</b>	<b>-11</b>

***FIG. 3***

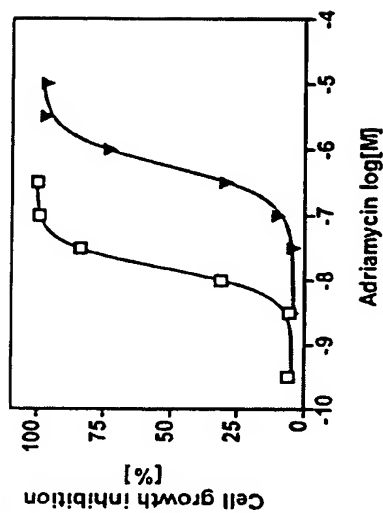
Cytotoxic activity of vincristine

on a human leukemia (LT12 and LT12/mdr)



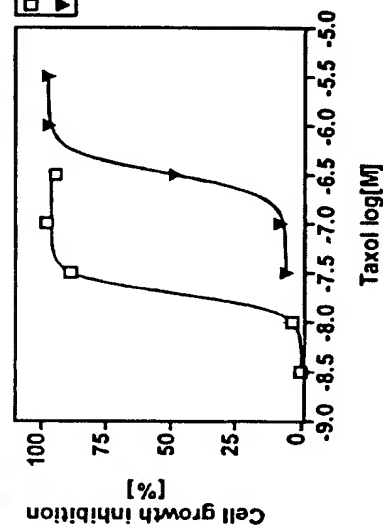
Cytotoxic activity of adriamycin

(doxorubicin) on a human leukemia (LT12 and LT12/mdr)



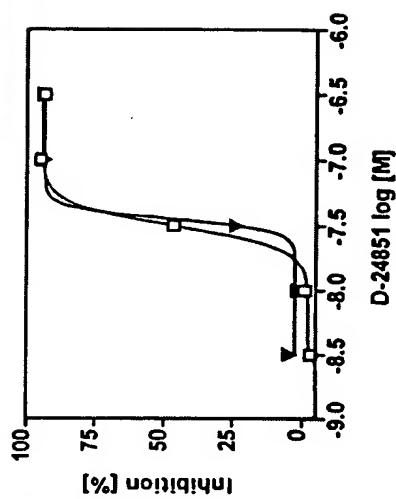
Cytotoxic activity of Taxol

on a human leukemia (LT12 and LT12/mdr)



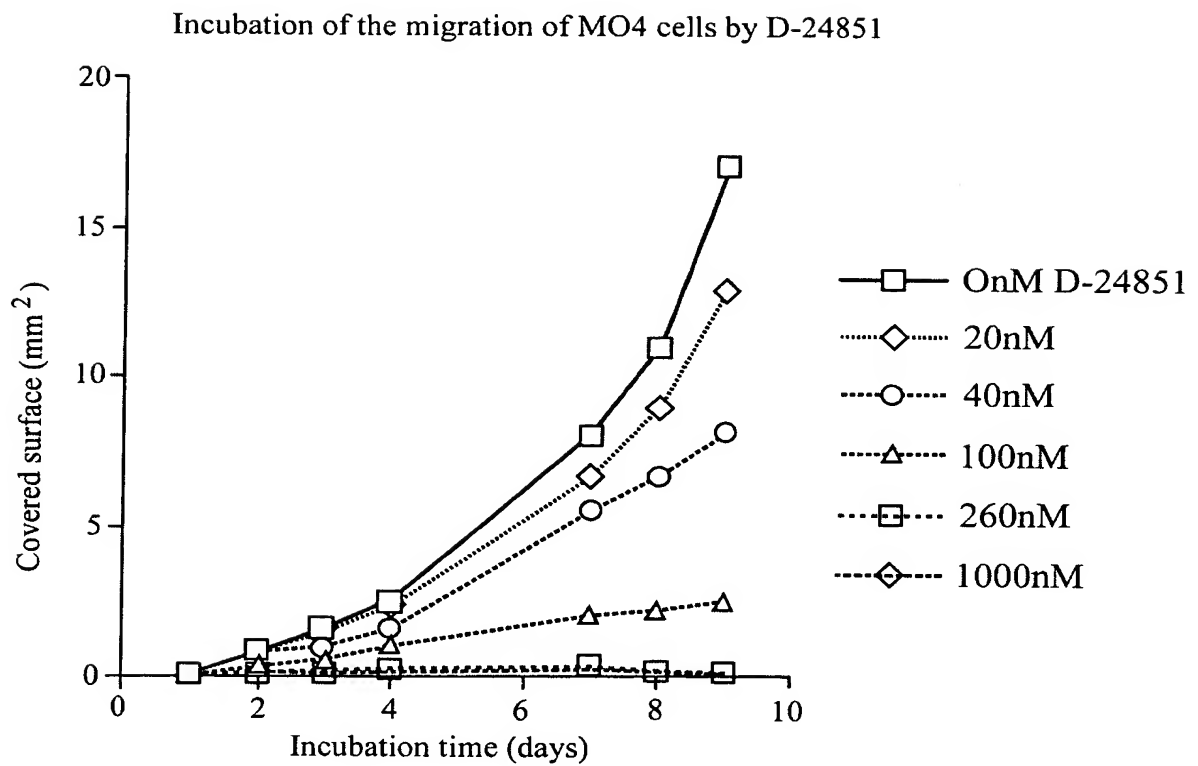
Cytotoxic activity of D-24851

on a human leukemia (LT12 and LT12/mdr)



**FIG. 4**

## ***FIG. 5***



- D-24851 inhibits the migration of MO4 cells in a dose-dependent manner  
From this, an antiinvasive and an antimetastatic action can be derived for D-24851.

Neurotoxicity

	D-24851 10x 20 mg/kg p.o	Vincristine 10x 0.2 mg/kg i.p.	Taxol 10x 15 mg/kg i.p.
Ataxia (rat)	--	+	++
Traction (rat)	--	+	++
Reaction (rat)	--	++	+++

+ p ≥ 0.05 vs. control

++ p ≥ 0.01 vs. control

-- = no effect

D-24851 shows no neurotoxicity [sic] in maximally antitumor-active doses in contrast to Taxol and vincristine

FIG. 6

Influence of D-24851 on the nerve conduction velocity (NCV) (rat)

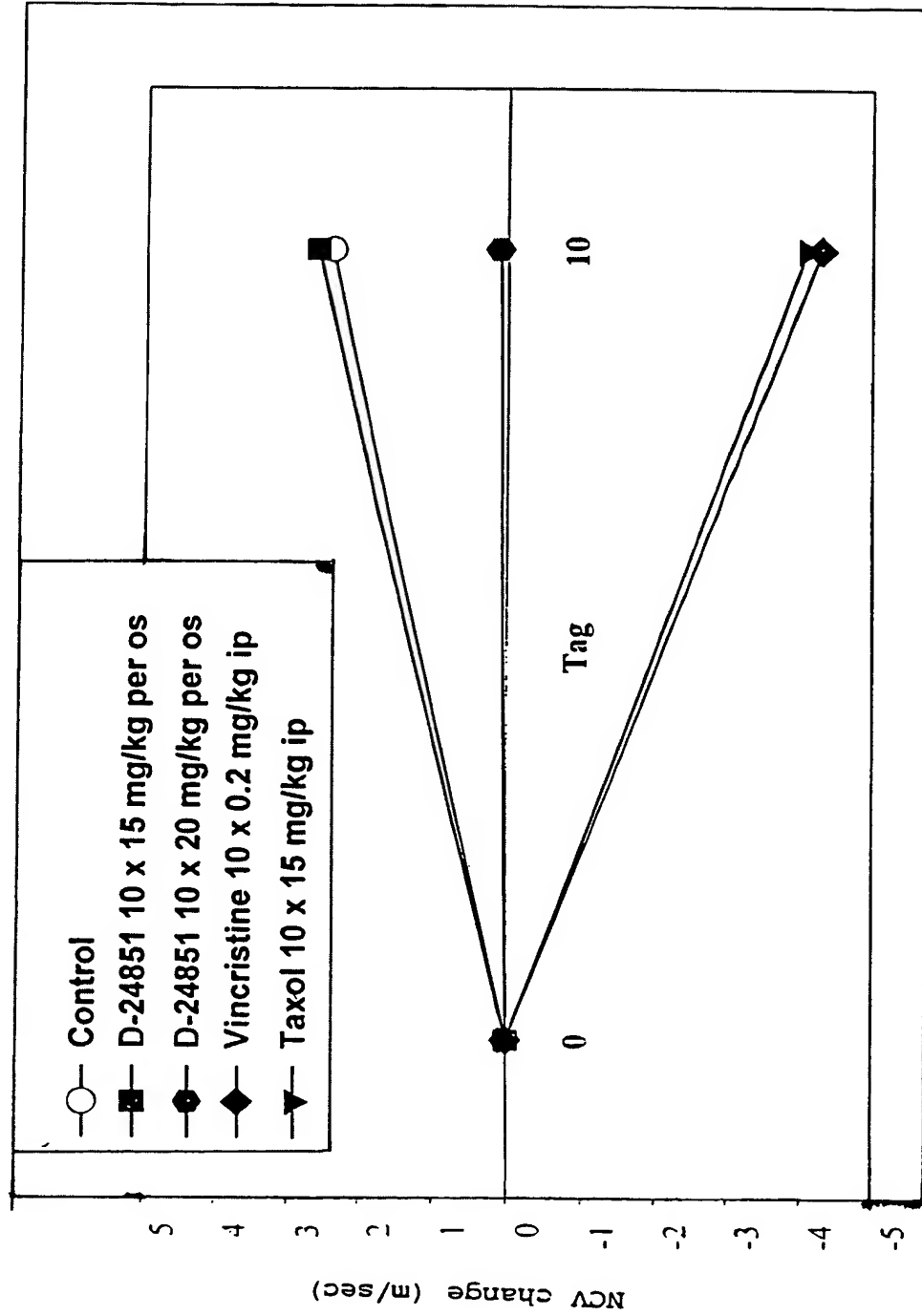
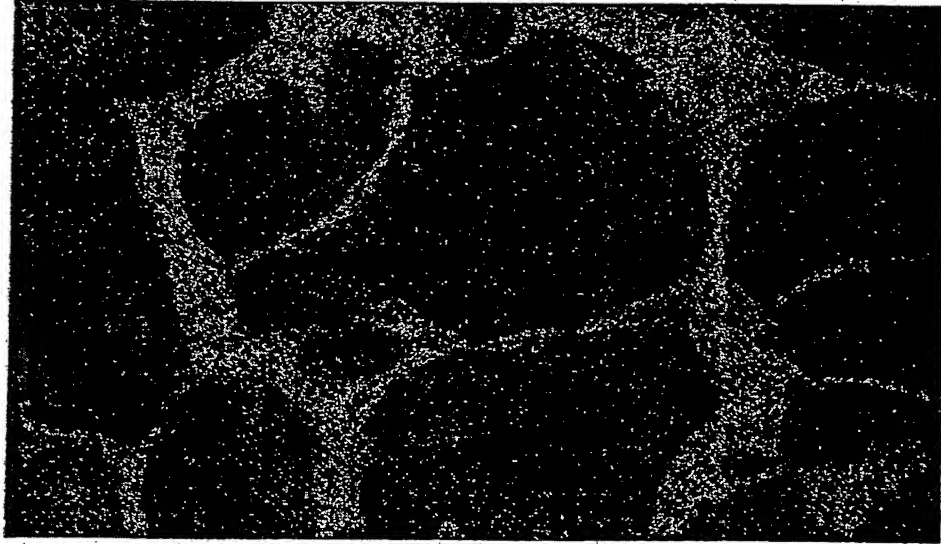


FIG. 7

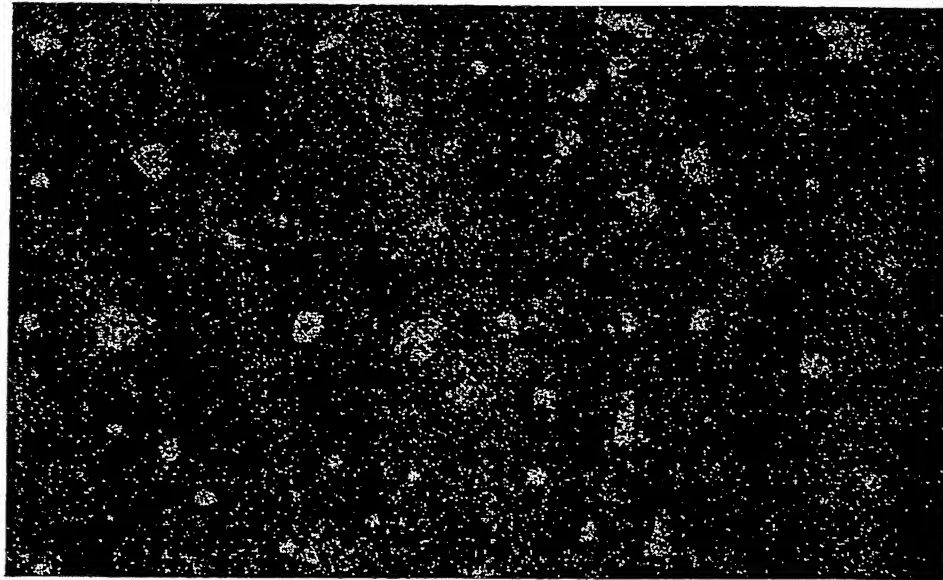
## ***FIG. 8***

Angiogenesis in human endothelial cell culture  
Vital staining, 44 hours after induction of angiogenesis

DMSO control



0.1  $\mu$ M D24851



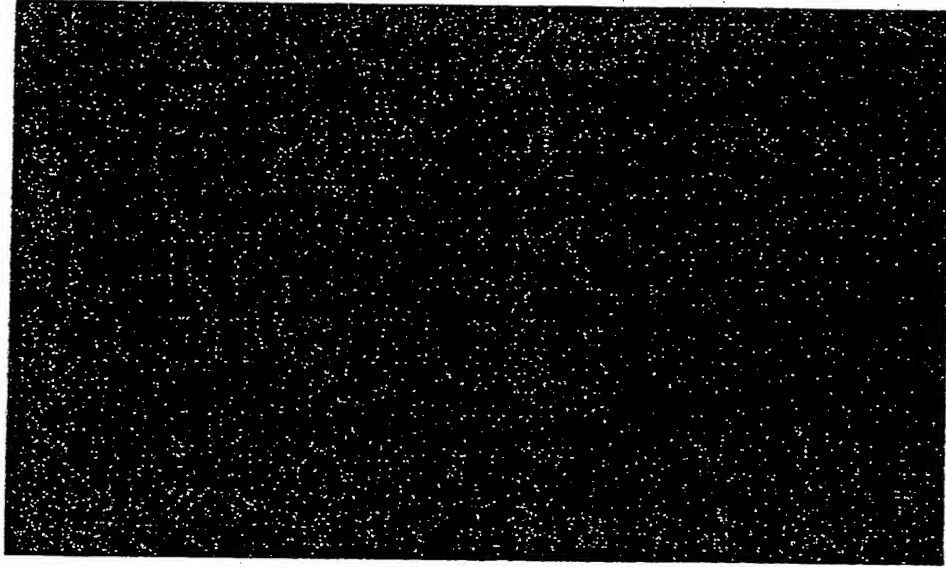


## ***FIG. 9***

Angiogenesis in human endothelial cell culture

Lethal staining, 22 hours after induction of angiogenesis

DMSO control



0.1  $\mu$ M D24851

